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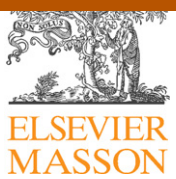

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CLINICAL RESEARCH

Results and predictors of early and late outcome of coronary artery bypass graft surgery in patients with ejection fraction less than 20%

Facteurs prédictifs à court et long termes des pontages chez les patients ayant une fraction d'éjection inférieure à 20 %

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KEYWORDS
CABG;
Low ejection fraction;
Poor left ventricular;
Mortality;
Survival

Summary
Background. — Severely depressed left ventricular ejection fraction (EF $\leq$ 20%) has historically been a major risk factor for morbidity and mortality in medically and surgically managed coronary artery disease. Recent studies have suggested that outcomes in patients with EF less or equal to 20% undergoing coronary artery bypass graft (CABG) surgery are improving, but the trend in the outcomes remains unclear.
Methods. — We retrospectively analysed prospectively collected data from 2909 consecutive patients undergoing isolated CABG between January 1998 and August 2006. One hundred and eighty five patients (6.4%) had an ejection fraction less or equal to 20%. Primary outcome measures for this study included hospital mortality, major postoperative complications, and long-term survival.
Results. — The median age in the overall patient population was 65 years (interquartile range 58—73) and 69% (n = 2015) of patients were male. The overall hospital mortality among our study population was 2.3% (n = 67). The mortality among patients with EF less or equal to 20 was 5% (n = 11) compared to 2% (n = 56) in patients with EF above 20% (p = 0.001). The proportion of patients with a high EuroSCORE (> 9%) was significantly greater in the group with EF less or equal to 20% (49%) than in the group with EF above 20% (20%). EF less or equal to 20% was not shown by multivariable logistic regression analysis to be an independent predictor of operative

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mortality. Survival rates at one year were 85 ± 2.8%, 93 ± 0.9%, and 98% ± 0.3% for patients with EF less or equal to 20%, over 20—40% and greater than 40% respectively; and at five years: 72 ± 0.4%, 81 ± 0.2% and 89 ± 0.1%, respectively ($p < 0.001$).
Conclusion. — We demonstrate acceptable mortality rates in patients with an EF less or equal to 20%, and show that EF less or equal to 20% does not appear to be an independent predictor of hospital mortality in our practice. Incremental changes in practice including improved patient selection and peroperative management may have reduced the impact of EF less or equal to 20% on mortality following CABG.

MOTS CLÉS
Pontages coronaires ;
Basse fraction d'éjection ;
Mortalité ;
Survie

Résumé
Introduction. — La fraction d'éjection (FEVG) très basse a toujours été un facteur de risque majeur de morbidité et mortalité chez les patients coronariens traités médicalement ou chirurgicalement. Des études récentes ont suggéré que le devenir des patients dont la FEVG inférieure ou égale à 20 % s'améliorait dans la dernière décade mais la tendance n'est pas certaine.
Méthode. — Nous avons analysé de manière rétrospective les données de 2909 patients consécutifs opérés de pontages coronaires isolés entre janvier 1998 et août 2006. Cent quatre-vingt cinq patients (6,4 %) avaient une fraction d'éjection inférieure ou égale à 20%. Les données concernant la mortalité et la morbidité opératoires ainsi que la survie à long terme ont été analysées.
Résultats. — L'âge moyen était de 65 ans (écart interquartile 58—73 ans) et 69% ($n = 2015$) étaient des hommes. La mortalité opératoire globale était de 2,3% ($n = 67$), 5 % ($n = 11$) dans le groupe de patients avec une FEVG inférieure ou égale à 20% et 2% ($n = 56$) chez les patients avec une FEVG supérieure à 20 % ($p = 0{,}001$). La proportion de patients avec un Euroscore supérieur à 9 était significativement plus importante chez les patients avec une FEVG inférieure ou égale à 20 % (49 % versus 20 %). La FEVG inférieure ou égale à 20 % n'était pas un facteur prédictif indépendant de mortalité opératoire en analyse multivariée. Les survies à un an des groupes avec une FEVG inférieure ou égale à 20 %, FEVG entre 20 et 40 % et FEVG supérieure à 40 % étaient de 85 ± 2,8 %, 93 ± 0,9 % et 98 ± 0,3 % et les survies à cinq ans de 72 ± 0,4 %, 81 ± 0,2 % et 89 ± 0,1 %, respectivement.
Conclusion. — La mortalité opératoire des pontages coronaires chez les patients avec une FEVG inférieure ou égale à 20% est acceptable. La FEVG inférieure ou égale à 20% n'apparaît pas être un facteur de mortalité opératoire dans notre exercice. Des améliorations sur la prise en charge des patients et des changements sur les indications ont permis de réduire l'impact des fractions d'éjection basses sur la mortalité après chirurgie de pontages coronaires.

Introduction

In patients with symptomatic multivessel coronary artery disease and severely depressed left ventricular (LV) function (ejection fraction [EF] less or equal to 20%), coronary artery bypass graft (CABG) surgery is the optimal therapeutic approach and remains superior to medical therapy [1—4]. The postoperative outcome of these patients has traditionally been worse than that of patients with moderate to good LV function [5,6]. More recent data, however, which report that EF less or equal to 20% does not appear to be an independent risk factor for operative mortality following CABG, indicates that incremental improvements in peroperative management and operative technique may have substantially reduced the negative impact of severely depressed LV function on early outcome [7].

There is, however, little data with respect to whether this is true for patients with very severely depressed LV function (EF $\leq$ 20%). Furthermore, the predictors of outcome in this high-risk group of patients are poorly defined, mainly because of the small number of individuals included in the majority of previous studies. Most clinical series have focused primarily on early operative mortality and morbidity, and there is little data describing long-term survival in this patient population. Herein, we report our clinical experience in a large, contemporary single centre series of patients with very severely depressed LV function who underwent CABG between 1998 and 2006. In this study we sought to determine the early outcome, predictors of early mortality and major postoperative complications as well as mid-term survival and predictors of late mortality following coronary revascularization in this patient population.

Materials and methods

Study population

We analysed a series of 2937 patients undergoing isolated CABG procedures at the Mount Sinai Medical Center between January 1998 and August 2006. Data were collected prospectively and analysed retrospectively.

The study group was determined by the preoperative EF. Patients with an EF less or equal to 20% formed the

study group, whereas those with an EF above 20% served as the control group. Patients undergoing reoperations or emergent procedures were included in this analysis. Patients admitted in cardiogenic shock undergoing a salvage procedure were excluded ($n = 28$). Preoperative EF was assessed by echocardiography ($n = 2240$, 77%), LV angiography ($n = 640$, 22%), and radionuclide studies ($n = 29$, 1%).

The protocol was approved by our local institutional review board and was compliant with the Health Insurance Portability and Accountability Act regulations and the ethical guidelines of the 1975 Declaration of Helsinki. The approval included a waiver of informed consent.

Data collection and outcome analysis

Clinical variables were entered prospectively into the New York State Department of Health (NYSDH, State Cardiac Advisory Committee) data registry. This registry represents a mandatory, verified, peer-reviewed data-collection system including all adult cardiac surgery procedures in the state of New York, and records and analysed data in a strictly supervised and widely reported fashion.

Patient demographics and risk factors, operative information and postoperative outcome data were analysed retrospectively. Additional information was obtained from patient charts when necessary. In addition, the logistic EuroSCORE was used for risk stratification [8]. The EuroSCORE is a risk-stratification system using multiple preoperative risk factors to predict operative mortality. Low to moderate risk was defined as a predicted mortality by EuroSCORE less or equal to 9%, whereas high risk was defined as a EuroSCORE above 9%.

Outcome measures for this study included hospital mortality, major postoperative complications (peroperative myocardial infarction, respiratory failure, renal failure, deep sternal wound infection, bleeding requiring reoperation, unplanned reoperation, stroke, and gastrointestinal complications), length of hospital stay and late survival. Hospital mortality was defined as death following the procedure before the patient's discharge regardless of the duration of hospitalization. Patients who died after discharge from hospital but within 30 days following the procedure were also considered as hospital deaths. Respiratory failure was defined as prolonged ventilator therapy (> 72 hours) or need for reintubation or tracheostomy. Renal failure was defined as creatinine above 2.5 mg/dL for more than seven postoperative days or the need for dialysis. Myocardial infarction was defined as the occurrence of a new Q-wave within 48 hours after surgery. Stroke was defined as a new permanent neurological event occurring peri- or postoperatively. Follow-up survival information was obtained by cross matching patients' social security numbers with the web-based social security death index.

Surgical management

All patients underwent a median sternotomy. Eighty six per cent ($n = 2493$) of procedures were performed utilizing cardiopulmonary bypass (CPB). The remaining 14% ($n = 416$) of procedures were performed without the use of CPB (off-pump coronary artery bypass, OPCAB). Since 2003, epiaortic ultrasonography was performed systematically in all patients to detect any atherosclerotic lesions of the ascending aorta prior to cannulation and clamping. The surgical strategy was tailored according to the presence or absence of calcification in the ascending aorta and its extent.

On-pump coronary revascularization

After systemic heparinization with an activated clotting time (ACT) level of at least 400 seconds, CPB was instituted between the ascending aorta and the right atrium using a two-stage cannula. Following aortic cross-clamp blood cardioplegia was administered in an antegrade and/or retrograde fashion. Since 2003, we routinely administered a solution of antegrade warm blood cardioplegia before removal of the aortic cross clamp (''hot-shot'' cardioplegia). Distal anastomoses were completed first followed by proximal anastomoses using the single aortic cross-clamp technique [9]. The left internal thoracic artery was routinely anastomosed to the left anterior descending artery. The aortic cross clamp was then released and the patients weaned from CPB after a short period of reperfusion. After the completion of CPB, protamine was given based on the heparin level.

Off-pump coronary revascularization

The procedure was performed based on the surgeon's preferences. This technique, however, was favoured particularly in patients with significant atherosclerotic disease of the ascending aorta. In patients undergoing OPCAB, heparin was administered to achieve an ACT of 300 seconds. Coronary stabilizer and cardiac positioning devices were used to access the coronary arteries under beating heart conditions. Intracoronary shunts were used systematically in all patients, in order to prevent prolonged myocardial ischaemia while distal anastomoses were created. Following completion of the procedure, protamine was administered based on the heparin level.

Statistical analyses

Normally distributed continuous variables are presented as mean $\pm$ standard deviation (SD) and otherwise as median and interquartile range (IQR). Categorical variables are shown as the percentage of the sample. A p-value less than 0.05 was considered as significant for all used statistical methods. The χ^2-test was used to evaluate potential confounders of the relationship between low EF and hospital mortality and morbidities. Stepwise multivariable logistic regression was then performed to assess the influence of low EF as an independent risk factor for hospital mortality and postoperative morbidities [10]. In patients with low EF, univariate and multivariable analyses were performed in the same manner to identify predictors of hospital mortality and late mortality.

The potential confounders introduced into multivariable analysis included age, sex, diabetes mellitus, congestive heart failure, previous cardiac procedure, body mass index, hypertension, myocardial infarction, chronic obstructive pulmonary disease, peripheral vascular disease, renal failure, hepatic failure, urgency of procedure and use of internal mammary artery.

Table 1 Patient demographics and risk factors ($n = 2909$).

	EF ≤ 20% ($n = 185$, 6.4%)	EF > 20% ($n = 2724$, 93.6%)	p
Mean age (years)	64 ± 10	66 ± 11	NS
Women, *n* (%)	54 (29)	840 (31)	NS
Mean body mass index (kg/m^2)	26 ± 5	27 ± 5	0.003
Body mass index > 30 kg/m^2, *n* (%)	31 (17)	652 (24)	0.017
Mean ejection fraction (%)	16 ± 4	48 ± 12	0.001
Congestive heart failure, *n* (%)	118 (64)	398 (15)	0.001
Previous myocardial infarction, *n* (%)	149 (80)	1280 (47)	0.001
Previous cerebrovascular accident, *n* (%)	18 (10)	219 (8)	NS
Peripheral vascular disease, *n* (%)	35 (20)	345 (13)	0.006
Diabetes, *n* (%)	81 (45)	1083 (40)	NS
COPD, *n* (%)	16 (9)	172 (6)	NS
Renal failure or dialysis, *n* (%)	14 (9)	123 (5)	0.015
Hypertension, *n* (%)	140 (75)	2155 (79)	NS
Aortic calcification-atherosclerosis, *n* (%)	9 (5)	133 (5)	NS
Previous cardiac operation, *n* (%)	11 (6)	96 (4)	NS
Previous PCI, *n* (%)	22 (12)	546 (20)	0.021
Coronary artery disease, *n* (%)			NS
One vessel	27 (15)	240 (11)	
Two vessel	36 (20)	496 (18)	
Three vessel	122 (65)	1938 (71)	
Emergent surgery, *n* (%)	21 (12)	131 (5)	0.001
Mean EuroSCORE (%)	14 ± 12	6 ± 7	0.001
Low (< 3%)	4 (3)	1050 (38)	
Moderate (3—9%)	91 (48)	1143 (42)	
High (9—25%)	63 (35)	446 (16)	
Very high (> 25%)	27 (14)	85 (4)	0.001

COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention.

Long-term survival of discharged patients was analysed using Kaplan-Meier survival curves. These analyses included the impact of low EF on survival following CABG in the overall population and the effect of preoperative risk factors and EuroSCORE on survival in the low EF group. Differences in patient characteristics were controlled by Cox proportional hazard analysis. The statistical analyses were performed with the use of SPSS 15 (SPSS Inc., Chicago, Il, USA).

Results

Demographic data and preoperative risk factors

The median age in the overall patient population was 65 (IQR 58—73) years and 69% (2015 of 2909) of patients were male. Very severely depressed LV function (EF ≤ 20%) was present in 185 (6.4%) patients.

There were significant differences in preoperative comorbidities between patients with EF less or equal to 20% and patients with EF above 20% (Table 1). Patients with EF less or equal to 20% were more likely to present with congestive heart failure ($p < 0.001$), a history of myocardial infarction ($p < 0.001$) or as an emergency ($p < 0.001$), and were more likely to have additional risk factors including peripheral vascular disease ($p < 0.006$) and renal failure ($p < 0.015$). The proportion of patients with a high or very high EuroSCORE (logistic EuroSCORE > 9%) was significantly greater in the EF less or equal to 20% group compared with the EF greater than 20% group (49% versus 20%, $p = 0.001$).

Operative characteristics

OPCAB was performed in 12% ($n = 24$) of low EF patients and in 14% ($n = 392$) of patients with normal LV function. The number of grafts in the low EF and control groups were 3.0 ± 1.4 and 3.2 ± 1.3, respectively, (p = NS). Patients with depressed LV function received significantly fewer internal mammary artery bypass grafts ($n = 123$, 65%) compared to the control group ($n = 2074$, 76%; $p = 0.003$). The cross clamp times were not significantly different between groups (Table 2). Twenty patients in the EF less than 20% group required an intra-aortic balloon pump (IABP; 10.8%) pre- or postoperatively, while 125 patients in the EF above 20% group had an IABP inserted ($p = 0.001$).

Mortality

The overall hospital mortality among our study population was 2.3% ($n = 67$). The mortality among low EF patients was 5.0% ($n = 11$) compared to 2.0% ($n = 56$) in those with EF above 20% ($p = 0.001$). For information, during the study period, 898 patients underwent non-emergent coronary

Table 2 Operative data.

	EF ≤ 20% (n = 185, 6.4%)	EF > 20% (n = 2724, 93.6%)	p
Off-pump procedures	24 (12)	392 (14)	NS
Mean number of grafts	3.0 ± 1.4	3.2 ± 1.3	NS
Use of left mammary artery, (%)	123 (65)	2074 (76)	0.003
Use of bilateral mammary arteries, (%)	6 (3)	308 (11)	0.001
Cardiopulmonary bypass time (min)	113 ± 51	104 ± 54	NS
Aortic cross-clamp time (min)	87 ± 74	82 ± 46	NS

bypass associated with other surgical procedures. In this particular population, operative mortality was 8.9% among patients with low EF (n = 90) and 6.7% among those with EF above 20% (n = 808).

Analysis of mortality rates over to two different periods (1998—2002 versus 2003—2006) showed that surgical mortality improved from 6.9% to 3.7% (p = 0.33) in the EF less than 20% group and from 2.8% to 1.2% (p = 0.002) in the control group.

Table 3 shows the risk factors for hospital mortality in the overall population after multivariable analysis. The presence of EF less or equal to 20% was not an independent predictor of hospital mortality (odds-ratio [OR] 1.39, 95% confidence interval [CI] 0.60—3.18, p = 0.441). Renal failure (OR 3.31, 95% CI 1.44—7.61, p = 0.005), peripheral vascular disease (OR 1.28, 95% CI 1.27—4.44, p = 0.007), cardiac reoperation (OR 4.13, 95% CI 1.64—10.82, p = 0.003) and a cardiopulmonary bypass time above 120 minutes (OR 2.47, 95% CI 1.13—5.39, p = 0.023) were independent predictors of hospital mortality.

The number of patients with very severely depressed LV function was too small to allow multivariable regression analysis to determine accurately independent predictors of hospital mortality.

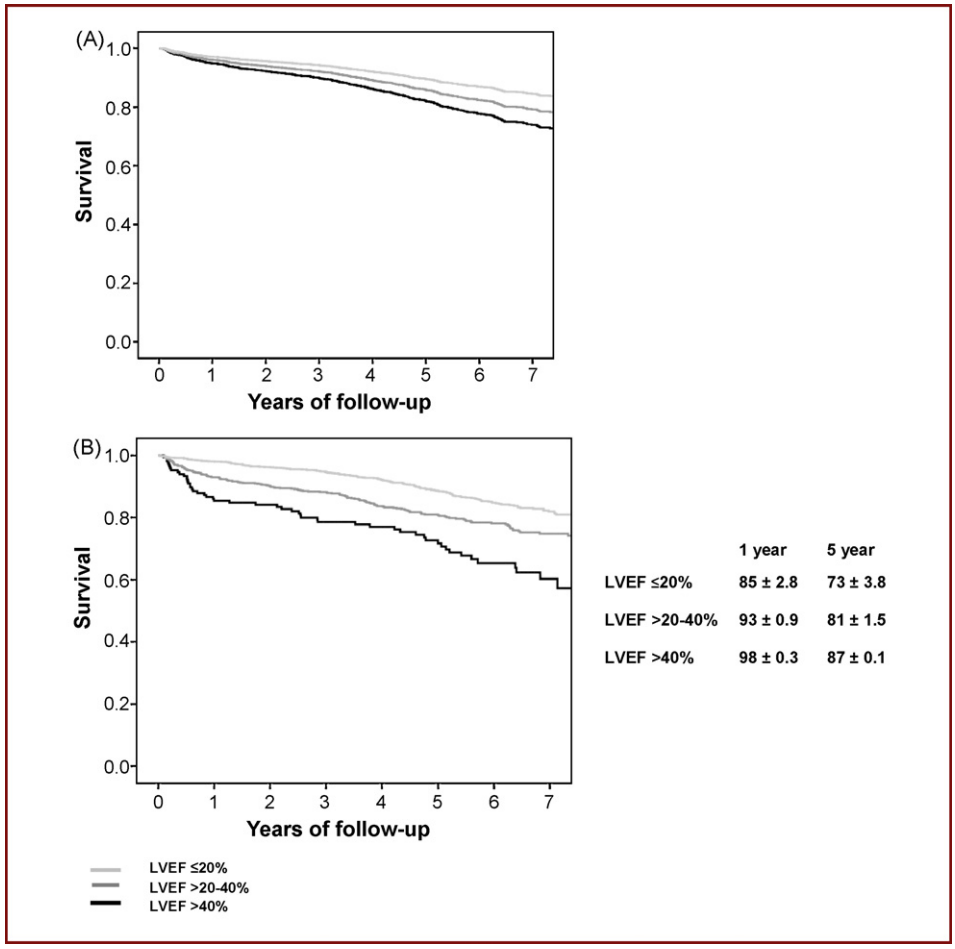

Figure 1. Kaplan-Meier survival curves. A. Adjusted for age, body mass index, congestive heart failure, peripheral vascular disease and chronic obstructive pulmonary disease by ejection fraction strata. B. Unadjusted survival curves.

Table 3 Predictors of hospital mortality in multivariable analysis.

Variable	Multivariate		
	OR	95.0% CI	*p*
Gender (female)	2.41	(1.35—4.30)	0.010
Age > 70 years	1.09	(0.60—1.99)	0.776
Ejection fraction ≤ 20%	1.39	(0.60—3.18)	0.441
BMI > 30	1.15	(0.60—2.22)	0.672
Congestive heart failure	1.89	(1.00—3.57)	0.050
Previous myocardial infarction	1.40	(0.76—2.58)	0.280
Previous stroke	0.73	(0.25—2.17)	0.571
Peripheral vascular disease	1.28	(1.27—4.44)	0.007
Diabetes mellitus	1.28	(0.71—2.27)	0.412
COPD	0.72	(0.24—2.17)	0.555
Renal failure	3.31	(1.44—7.61)	0.005
IABP	3.85	(1.44—7.61)	0.002
Hemodynamic unstability	2.29	(0.79—6.61)	0.125
Hypertension	1.66	(0.68—4.01)	0.264
Reoperation	4.13	(1.64—10.82)	0.003
X-Clamp Time > 80 min	0.87	(0.39—2.04)	0.740
CPB Time > 120 min	2.47	(1.13—5.39)	0.023

BMI: body mass index; CI: confidence interval; COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; IABP: intra-aortic balloon pump; OR: odds-ratio.

Morbidity

Postoperative complications following CABG among the overall study population included stroke ($n = 47$, 1.6%), myocardial infarction ($n = 22$, 0.8%), renal failure requiring dialysis ($n = 27$, 0.9%) deep sternal wound infection ($n = 40$, 1.4%) sepsis ($n = 43$, 1.5%), reoperation for bleeding ($n = 57$, 1.9%) and respiratory failure ($n = 176$, 6.0%). Patients with EF less or equal to 20% had a significantly higher rate of postoperative renal failure ($p = 0.027$), and sepsis ($p = 0.001$) compared to patients with normal LV function (Table 4). In multivariable logistic regression analysis EF less or equal to 20% was shown to be an independent predictor of postoperative renal failure (OR 2.74, 95% CI 1.06—5.84, $p = 0.042$) and sepsis (OR 3.71, 95% CI 1.60—8.60, $p = 0.002$) (Table 5).

Long-term survival

The mean follow up time was 4.2 ± 2.5 years. Long-term survival of discharged patients was significantly decreased in patients with severely depressed LV function compared to those with EF above 20% (Figs. 1 and 2). One-year survival rates were $85 \pm 2.8\%$, $93 \pm 0.9\%$, and $98 \pm 0.3\%$ for patients with EF less or equal to 20%, above 20—40% and above 40%, respectively; five-year survival rates were $72 \pm 0.4\%$, $81 \pm 0.2\%$ and $89 \pm 0.1\%$, respectively ($p < 0.001$). Late survivors were significantly less likely than non-survivors to have a very high preoperative predicted risk by the EuroSCORE (12% versus 23%, respectively, $p = 0.009$). The numbers of patients were too small to permit multivariable analysis determining whether EuroSCORE was an independent predictor of late mortality.

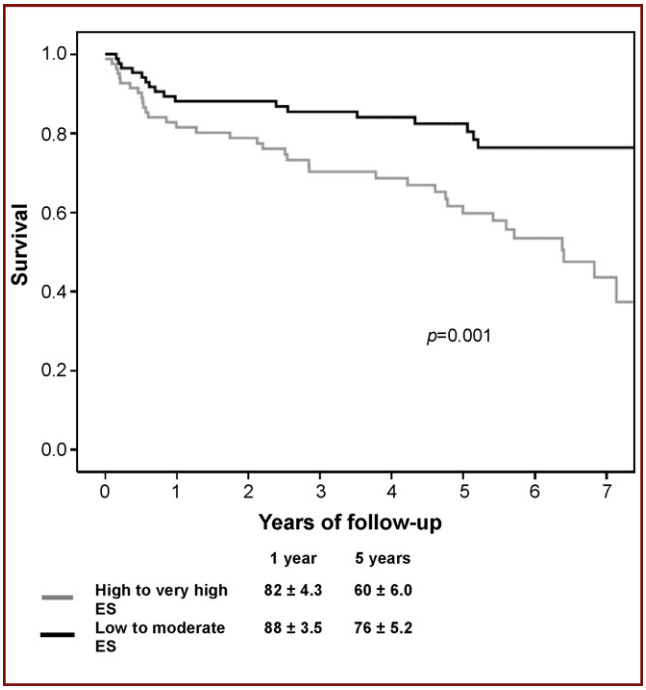

Figure 2. Late survival Kaplan-Meier curves in the low ejection fraction group by EuroSCORE strata (ES).

Discussion

This is one of the largest, contemporary, single-centre series analysing the outcomes of patients with very severely depressed LV function (EF ≤ 20%) undergoing CABG. The main findings of this study include a very low operative

Table 4 Mortality and morbidities in the overall population ($n = 2909$).

	EF ≤ 20% ($n = 185$, 6.4%)	EF > 20% ($n = 2724$, 93.6%)	p
Hospital mortality	11 (5)	56 (2)	0.001
Morbidities			
Postoperative stroke	5 (3)	42 (1)	NS
Postoperative myocardial infarction	4 (2)	18 (1)	0.049
Postoperative renal failure-dialysis	5 (3)	22 (1)	0.027
Respiratory failure	27 (14)	149 (5)	0.001
Deep sternal wound infection	3 (2)	37 (1)	NS
Postoperative systemic infection	10 (5)	33 (1)	0.001
Re-exploration for bleeding	9 (5)	48 (2)	0.010
Gastrointestinal complications	3 (2)	26 (1)	NS
Length of stay in days (interquartile range)	9 (6—15)	6 (5—9)	0.001

mortality in this group of high-risk patients. We show that very severely depressed LV function does not appear to be an independent predictor of early mortality in patients undergoing CABG in our practice, although it remains an independent risk factor for major morbidity postoperatively and for late mortality. We show for the first time that the EuroSCORE is an accurate predictor of long-term survival in this high-risk group of patients.

Prevalence of low EF in CABG patients

The reported prevalence of severe LV dysfunction in patients undergoing CABG in large series and registries has ranged from 3.4—15% [6,11], reflecting the fact that definitions of LV dysfunction vary widely, with most studies choosing an EF of less or equal to 30% [6,11—18], and a few using higher values [19,20]. Both Parsonnet and EuroSCORE risk-stratification systems define poor ventricular function as an EF less than 30% [5]. Improving outcomes in patients with borderline poor ventricular function has focused attention on the results of surgery in patients at the most compromised end of the scale, with EF less or equal to 20%. The prevalence of EF less or equal to 20% in an analysis of a large registry of patients undergoing CABG between 1990 and 2001 ranged between 2.3 and 3.1% [7]. The prevalence of EF less or equal to 20% in our cohort of patients was over double this at 6.4%, which may reflect the continuing wider trend of higher numbers of patients with very severely LV dysfunction being referred for cardiac surgery [21], as well as a referral bias at our institution.

Mortality and morbidity

Patients with very severe LV dysfunction undergoing CABG have been consistently shown in the literature to have higher operative mortality and reduced long-term survival compared to patients with normal or mildly impaired LV. The hospital mortality reported in patients with EF less or equal to 30% during the late 1980s was as high as 20% [1,22]. This has decreased significantly: the majority of series of patients with low EF undergoing CABG in the 1990s reported early mortalities between 5 and 15% [3,6,7,11—14,19,23—28], whereas the majority of series describing results in patients operated on after 2000 were reporting mortalities of less than 5% [17,29].

Few contemporary studies report the results of CABG in patients with EF less or equal to 20%. The mortality reported in patients operated on between 1997 and 1999 by the New York State cardiac surgery database study was 6.5% in hospital, with a 4.6% early mortality in patients with EF less or equal to 20% [6]. More recent data from the registry study by Daveierwala et al. reported a hospital mortality rate of 8.9% in this group of patients operated on between 1998 and 2001, compared to 10.9% in patients operated on between 1990 and 1993 [7]. Our results comparing two periods of surgical practice (1998—2002 versus 2003—2006) reflect the improvement in mortality reported in the literature in recent years,

Table 5 Multivariable logistic regression analysis of EF less than 20% as an independent predictor of major postoperative morbidities.

	Multivariate		
	OR	95.0% CI	p
Postoperative stroke	0.35	(0.43—2.78)	0.318
Postoperative myocardial infarction	2.75	(0.71—10.49)	0.139
Postoperative renal failure — dialysis	2.74	(1.06-5.84)	0.042
Respiratory failure	2.89	(0.93—1.64)	0.087
Deep sternal wound infection	4.50	(0.33—1.28)	0.758
Postoperative systemic infection	3.71	(1.60—8.60)	0.002
Reexploration for bleeding	2.55	(0.83—6.11)	0.111
Gastrointestinal complications	1.34	(0.35—5.15)	0.666

even if it was not statistically significant in the EF less than 20% group, probably due to the small sample size.

This improvement in operative outcome is certainly multifactorial and probably related to improvements in myocardial protection strategies and perioperative management of related comorbidities, as well as improved case selection involving myocardial viability studies. During the study period intraoperative epiaortic and transoesophageal echocardiography, blood cardioplegia with warm induction and reperfusion, and modern postoperative management protocols became standard adjuncts to surgical practice. Despite the fact that our study was not designed to give information with respect to the many incremental changes in operative and perioperative management that occurred since its inception, we believe that these have made a significant contribution to the reduction in operative mortality.

EF less or equal to 20% was not shown by multivariable logistic regression analysis of our patient database to be an independent risk factor for early mortality (OR 1.39, 95% CI 0.60—3.18, $p = 0.44$). Historically, severely depressed LV function has been identified as an independent risk factor for early mortality [7,30,31]. Recent studies have suggested that the significance severely depressed LV function as a predictor of mortality may be decreasing: OR for severely depressed LV function did not reach statistical significance in multivariable logistic regression analysis of two large, contemporary series of patients. The differences in definitions of severely depressed LV may partly account for this (Hillis et al. [19] included patients with EF less or equal to 35%). The study by Davierwala et al., [7] however, which looked at a registry of patients undergoing CABG over three time periods between 1990 and 2001, and which defined severely depressed LV function as EF less than 20% showed that the impact of EF less than 20% on early mortality declined across the three periods, so that in the third it was no longer an independent predictor by multivariable analysis of hospital mortality. This decline in the predictive value of severely depressed LV function lends further support to the hypothesis that evolution in case selection, operative and perioperative management has significantly improved outcomes in these traditionally high risk patients.

Severely depressed LV function has previously been associated with postoperative respiratory failure, renal failure and dialysis, sepsis and gastrointestinal problems [6,30]. Our analysis showed that patients with EF less or equal to 20% undergoing CABG had a significantly higher rate of postoperative respiratory failure ($p < 0.05$) and sepsis ($p < 0.05$) than patients with EF above 20%, and multivariable logistic regression analysis confirms that EF less or equal to 20% was an independent risk factor for these complications in our patient group.

Long-term survival

Patients with EF less or equal to 20% in our study had an actuarial one-year survival of 85.0%, and a five-year survival of 72.7%, significantly poorer than that of patients with EF above 20%. When divided into a high- and lower-risk group by logistic EuroSCORE, patients with a low to moderate predicted risk (< 9%) by EuroSCORE had one- and five-year survivals of 88 and 76%, respectively, compared to 82% and 60%, respectively, for patients with EuroSCORE above 9%

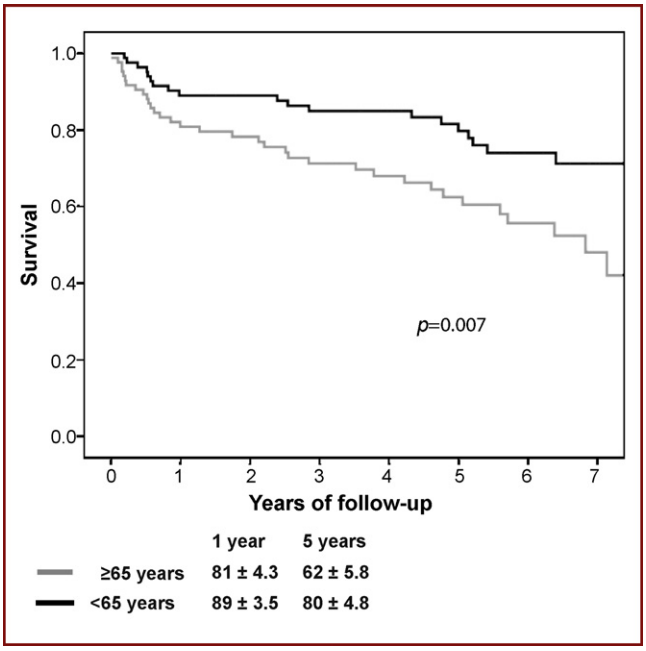

Figure 3. Late-survival Kaplan-Meier curves by age strata.

($p < 0.001$; Fig. 2). These figures are at the upper limit of the long-term survival data recorded in the literature. One-year survivals reported in single centre and registry studies analysing patients with EF less or equal to 30 undergoing CABG within the past decade range from 81 to 92% [17], three-year survival ranges from 68 [32] to 87% [17], and five-year survival where reported ranges from 45 [32] to 78% [16]. The strongest predictors of mortality during long-term follow-up were age greater or equal to 65 years and a history of chronic obstructive pulmonary disease, with less than half of patients in the EF less or equal to 20% group with either of these risk factors surviving more than 5 years (Table 6, Figs. 3 and 4). It appears from these figures that the increasingly high-risk patient profile may negate any benefit on long-term survival gained by improvements in early outcome. Comparative data from the literature are, however, not risk adjusted and comparisons are therefore difficult to make.

Limitations

This is the one of the largest contemporary, single-centre analyses of outcomes in patients with EF less or equal to 20% undergoing CABG. This study does, however, present certain limitations. Firstly, given that this is a retrospective observational study, conclusions are necessarily limited in their application. Secondly, clinical outcomes are limited to major postoperative morbidity and mortality with no information on late complications, quality of life, cause of death during follow-up, postoperative EF (including measures of improved myocardial viability) or cost-analysis. The lack of data with respect to specific changes in operative and peroperative practice makes it difficult to draw any firm conclusions that could direct future practice. Finally, the wide variation in definitions of severely depressed LV function highlighted above, as well as the lack of risk stratification in the literature means that it is difficult to draw

Table 6 Late-survival patient characteristics.

	All patients($n=174$)	Alive($n=121$)	Died($n=53$)	p
Mean age (years)	64 ± 10	62.9 ± 10.6	67.9 ± 10.9	0.004
Women, *n* (%)	48 (28)	30 (25)	18 (34)	NS
Mean body mass index (kg/m^2)	26 ± 5	26.7 ± 5.1	25.1 ± 4.4	0.046
Body mass index > 30 kg/m^2, *n* (%)	29 (17)	23 (19)	6 (11)	NS
Congestive heart failure, *n* (%)	110 (63)	71 (59)	39 (73)	0.043
Previous myocardial infarction, *n* (%)	139 (80)	94 (78)	45 (85)	NS
Previous cerebrovascular accident, *n* (%)	18 (10)	10 (8)	8 (15)	NS
Peripheral vascular disease, *n* (%)	31 (18)	16 (13)	15 (28)	0.017
Diabetes, *n* (%)	75 (43)	53 (44)	22 (41)	NS
COPD, *n* (%)	15 (9)	6 (5)	9 (17)	0.013
Renal failure or dialysis, *n* (%)	13 (7)	9 (7)	4 (7)	NS
Hypertension, *n* (%)	130 (75)	90 (74)	40 (75)	NS
Aortic calcification-atherosclerosis, *n* (%)	8 (5)	2 (2)	6 (12)	0.011
Previous cardiac operation, *n* (%)	19 (10)	15 (12)	4 (8)	NS
Previous PCI, *n* (%)	22 (12)	16 (12)	6 (11)	NS
Coronary artery disease, *n* (%)				NS
One vessel	24 (14)	13 (11)	11 (20)	
Two vessel	37 (21)	26 (21)	11 (17)	
Three vessel	113 (65)	82 (68)	31 (63)	
Emergent surgery, *n* (%)	19 (11)	13 (11)	6 (11)	NS
Mean EuroSCORE (%)	14 ± 12	12 ± 12	17 ± 11	0.020
Low (< 3%)	4 (2)	3 (2)	1 (2)	
Mod (3—9%)	85 (49)	69 (57)	16 (30)	
High (9—25%)	62 (36)	37 (31)	25 (47)	
Very high (> 25%)	23 (13)	12 (10)	11 (21)	0.009

COPD: chronic obstructive pulmonary disease; NS: not significant; PCI: percutaneous coronary intervention.

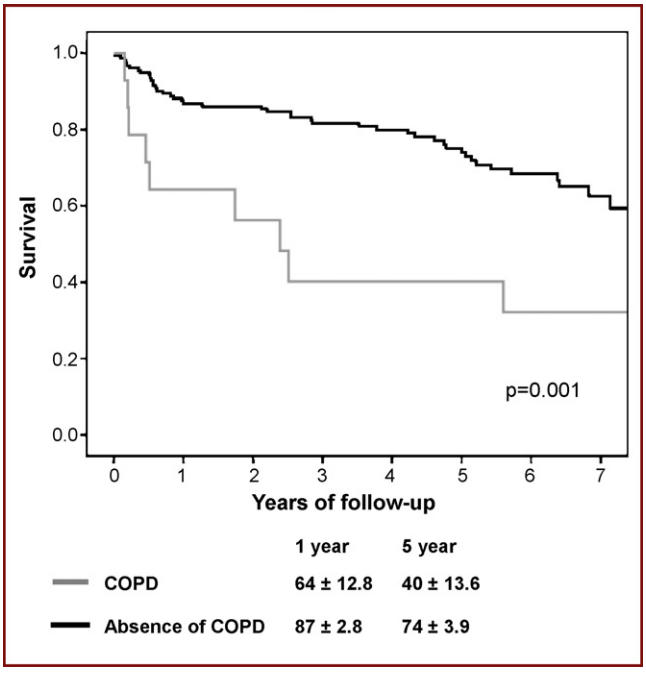

Figure 4. Late-survival Kaplan-Meier curves by chronic obstructive pulmonary disease strata.

accurate comparisons between the outcomes of studies in this area.

Conclusion

Excellent results following CABG can be expected in patients with EF less or equal to 20%, with minimal increases in postoperative morbidity and mortality. Contemporary results in this high-risk patient group are substantially better than historical reports despite a substantial increase in the burden of comorbidities and predicted mortality. Very low EF does not appear to be an independent risk factor for early mortality, but long-term survival is still significantly reduced when compared with patients with EF above 20%. Careful preoperative selection and peroperative management, including optimal strategies of myocardial preservation, is essential in patients with EF less or equal to 20% undergoing cardiac surgery.

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